

All solvents are HPLC grade. MS spectra are obtained by API 2000 LC/MS/MS system. ¹H-NMR data are from Analysis Center of East China University of Science and Technology. All starting materials are publicly available in the market.

5 Synthesis of 4-(4-Methylbenzyl)-4'-hydroxybiphenyl-4-carboxylate
4-Methyl-4'-hydroxybiphenyl-4-carboxylate

A solution of 4-(4-hydroxyphenyl) benzoic acid 21.4g (0.1mol) in 500mL absolute methanol in a flask equipped Soxhlet apparatus filled with A4 molecular sieve. Then dropped 2.0mL concentrated sulfuric acid. The mixture refluxed for 72hrs. After
10 removal the solvent by vacuum, the residual oil dissolved in 100mL toluene, washed to pH=7 with water. The organic layer was dried by MgSO₄ and filtered. The obtained filter liquor was added a certain quantity of activated charcoal and heated to reflux for 10~15min and filtered. Removed the solvent to obtain a white crystal, 4-Methyl-4'-hydroxybiphenyl-4-carboxylate 18.2g (yield 80%).

15 4-(4-Methylbenzyl)-4'-hydroxybiphenyl-4-carboxylate

A suspension of 4-Methyl-4-hydroxybiphenyl-4-carboxylate 9.0g (40.0mmol), 4-methylbenzylalcohol 24.4g (200.0mmol), sodium methoxide 1.0g (4.0mmol), toluene 20.0mL, under N₂ prevention, was heated to reflux 2.5hrs. During the reaction, added
20 additional 20.0mL toluene in order to bring out the resultant methanol under reflux. Then cooled to room temperature, added 10mL acetic acid and ice 40g to adjust the pH=5. The obtained organic layer was concentrated under reduced pressure to remove solvent and the excess 4-methylbenzylalcohol. Cooled to obtain brownish oil. Stood to produce the crude crystals slowly. Recrystallized from toluene/n-hexane to give a white crystal, 4-(4-methylbenzyl)-4'-hydroxybiphenyl-4-carboxylate 7.3g (yield 71%).

25 ¹H-NMR(500MHz,CDCl₃): δ2.35(s, 3H), 5.35(s, 2H), 6.90(d, 2H), 7.15(d, 2H), 7.35(d, 2H), 7.50(d, 2H), 7.60(d, 2H), 8.10(d, 2H)

30 Synthesis of 4-guanidinoalkylbenzoic acid hydrochloride

4-Guanidinomethyl benzoic acid hydrochloride

2N NaOH solution 72mL was added to a solution of methyl isothiurea disulfate 20.0g (0.14mol) in 36mL water with cooling in ice bath, and stirred. Then 21.0g

(0.138mol) 4-aminomethylbenzoic acid in 140mL 2N NaOH solution was added dropwise. The mixture was left to stand overnight at room temperature and then chilled in ice water for 1hr. The precipitated white crystals were filtered off and washed with cold water. The filtrate was dissolve in warm 1N HCl and insoluble material was removed by filtration. The solution was concentrated in vacuum to crystallize. The colorless prisms crystallized when the solution was cooled, then filtered and dried, gave 4-guanidinomethylbenzoic acid hydrochloride 22.1g(yield 70%).
LC/MS=194(M+H)

4-Guanidino benzoic acid hydrochloride

2N NaOH solution 36mL was added to a solution of methyl isothiurea disulfate 10.0g (0.07mol) in 36mL water with cooling in ice bath, and stirred, then 9.5g (0.069mol) 4-aminomethylbenzoic acid in 2N NaOH solution 70mL was added dropwise. The mixture was left to stand overnight at room temperature and then chilled in ice water for 1hr. The precipitated white crystals were filtered off and washed with cold water. The filtrate was dissolve in warm 1N HCl and insoluble material was removed by filtration. The solution was concentrated in vacuum to crystallize. The colorless prisms crystallized when the solution was cooled, then filtered and dried, gave 4-guanidinobenzoic acid hydrochloride 10.0g (yield 67%).
LC/MS=180(M+H)

Synthesis of 4-guanidinoalkyl benzoate

4-(4-methylbenzyl)-4'-[guanidinomethylbenzoyloxy] biphenyl-4-carboxylate hydrochloride

A suspension of 4-methylbenzyl-4'-hydroxybiphenyl-4-carboxylate, 2.42g(0.010mol), 4-Guanidinomethyl benzoic acid hydrochloride 2.3g (0.010mol) and dicyclohexylcabodiimide 4.1g(0.020mol) in pyridine 150ml was stirred at room temperature for 48hrs, after removed of insoluble materials by filtration. The filtrate was evaporated to dryness and residue solid was treated with 0.1N hydrochloric acid (50mL) and ether (50mL), The aqueous layer was washed with ether again and concentrated to 20ml, the resulting crystals were recrystallized in ethanol/hexane, gave 4-(4-

methybenzyl)-4'[guanidinomethylbenzoyloxy] biphenyl -4-carboxylate Hydrochloride
2.9g (yield 55%).

LC/MS=494(M+H)

5 4-(4-methylbenzyl)-4'-[guanidinobenzoyloxy] biphenyl-4-carboxylate hydrochloride

A suspension of 4-methylbenzyl-4'-hydroxybiphenyl-4-carboxylate,
2.42g(0.010mol), 4-Guanidinobenzoic acid hydrochloride 2.2g (0.010mol) and
dicyclohexylcabodiimide 4.1g(0.020mol) in pyridine 150ml was stirred at room
temperature for 48hrs, after removed of insoluble materials by filtration. The filtrate was
10 evaporated to dryness and residue solid was treated with 0.1N hydrochloric acid (50mL)
and ether (50mL), The aqueous layer was washed with ether again and concentrated to
20ml, the resulting crystals were recrystallized in ethanol/hexane, gave 4-(4-
methybenzyl)-4'-[guanidinobenzoyloxy] biphenyl-4-carboxylate
Hydrochloride 3.0g(yield 60%).

15 LC/MS=482(M+H)

4-Phenyl-4'-guanidinomethylbenzoate hydrochloride

A suspension of 4-guanidinomethylbenzoic acid hydrochloride 2.3g (0.010mol),
phenol 1.0g (0.011mol) and dicyclohexylcarbodimide 4.1g (0.020mol) in pyridine
20 (150ml) was stirred at room temperature for 48hrs. After removal of insoluble materials
by filtration, the filtrate was evaporated to dryness and residual solid was treated with
0.1N hydrochloric acid (50ml),washed with ether. The aqueous layer was concentrated
to 20ml, the resulting crystals were filtered and washed with isopropanol / isopropyl
ether, gave 4-Phenyl-4'- guanidinomethylbenzoate hydrochloride 2.3g (yield 75%).

25 LC/MS=269(M+H)

4-Phenyl-4'-guanidinobenzoate hydrochloride

A suspension of 4-guanidinobenzoic acid hydrochloride 2.2g (0.010mol), phenol
1.0g (0.011mol) and dicyclohexylcarbodimide 4.1g (0.020mol) in pyridine (150ml) was
30 stirred at room temperature for 48hrs. After removal of insoluble materials by filtration,
the filtrate was evaporated to dryness and residual solid was treated with 0.1N
hydrochloric acid (50ml), washed with ether. The aqueous layer was concentrated to